U.S.S.N. 09/661,773
Filed: September 14, 2000
AMENDMENT

11. (amended) The composition of claim 1 wherein the polyhydroxyalkanoate has a molecular weight of less than 100,000 as determined by gel permeation chromatography.

12. (amended) The composition of claim 11 wherein the molecular weight is less than 50,000 as determined by gel permeation chromatography.

15. (amended) The composition of claim 1 further comprising [an agent selected from the group consisting of dyes, compounds with anti-microbial activity, anesthetics, adjuvants, anti-inflammatory compounds, surfactants, steroids, lipids, enzymes, antibodies, and hormones] a bioactive agent.

Please cancel claims 18-28.

29. (amended) A composition suitable for use in the treatment of osteoarthritic knees comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate, wherein the composition is suitable for use as a viscosupplement

31. (amended) A kit [of parts] comprising

(a) the composition of claim 1; and

(b) a means for delivering the composition to a patient.

Remarks

Response to Restriction Requirement

The claims were divided into three groups, Group I, claims 1-17 and 29-32, drawn to a composition for the repair or augmentation of tissue, and for the treatment of osteoarthritic knees, comprising a biocompatible, bioabsorbable fluid which comprises a

polyhydroxyalkanoate, Group II, claims 18-24, drawn to methods for repairing, contouring, or augmenting tissue, using the composition, and Group III, claims 25-28, drawn to methods for treating osteoarthritic knees, using the composition. Applicants elected claims 1-17 and 29-32. Claims 18-28 have now been canceled.

Rejections under 35 U.S.C. 112

Claims 7, 11, 12, 29 and 31 were rejected under 35 U.S.C. 112, second paragraph as indefinite. These rejections are respectfully traversed if applied to the amended claims.

Claim 7 was amended to depend from claim 5.

Claims 11 and 12 were amended to recite the method of determining molecular weight. Support is found in Table 1 and Table 2 – see page 14, for example.

Claim 15 has been amended to delete the Markush group, and to insert "bioactive agent" in place thereof. Support is found at page 11, lines 25-26. This avoids the problem with the improper Markush claim containing overlapping elements. The application is clearly enabling for inclusion of bioactive agents. The burden is on the examiner to provide some reason, not just unsubstantiated argument, why one could not make and use the polyhydroxyalkanoates including a bioactive agent, and no such evidence has been provided.

Claim 29 is drawn to a composition, not a use. The claim has been amended to recite that the composition is suitable for use, rather than is for use, in treating arthritic knees.

Claim 31 has been amended to delete "of parts"

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Rejections under 35 U.S.C. 102

Claims 1-17 and 29-32 were rejected under 35 U.S.C. 102(e) as disclosed by U.S. Patent No. 6,277,431 to Sankaram. Claims 1-17 and 29-32 were rejected under 35 U.S.C. 102(b) as disclosed by WO 96/00263 to Stichting Ondersoek en Ontwikkeling Noord Nederland (Eggink). Claims 1-17 and 29-32 were also rejected under 35 U.S.C. 102(b) as disclosed by WO 91/13207 to Marchessault. Claims 1-17 and 29-32 were rejected under 35 U.S.C. 102(a) as disclosed by WO 99/32536 by Martin. Claims 1-17 and 29-32 were rejected under 35 U.S.C. 102(a) as disclosed by WO 98/51812 by Williams. These rejections are respectfully traversed.

The claims in this application are drawn to a composition for the repair or augmentation of tissue in an animal or human, comprising a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate. Claim 1 has been amended to more specifically recite that the fluid is injectable into a human or animal. Support is found in the application at page 12, lines 1-6 and page 4, lines 2-6.

Sankaram

Sankaram, in contrast, discloses microspheres which include both polymer and lipid components, which can be suspended in water (col. 2, line 67 to col. 3, line 1). It is acknowledged that one of many types of polymers that could be used is a polyhydroxyalkanoate. Sankaram states that the material is suitable for drug delivery (col. 9). Col. 9, lines 17-20 noted by the examiner does not teach that the material is administered to cells or tissue, but that the material which is encapsulated for delivery include "Prodrugs which undergo conversion to the

indicated physiologically active substances upon local interactions with the intracellular medium, cells, or tissues".

There is no disclosure of a composition suitable for the repair or augmentation of tissue in an animal or human, as claimed, Therefore Sankaram does not disclose each and every feature of the claimed composition.

Eggink

Eggink discloses a polyhydroxyalkanoate in the form of an elastomeric film, which is prepared from an aqueous dispersion of a polyhydroxyalkanoate. Claims 1 and 5-6 do not refer to injection via a kit. The abstract refers to a coating of materials to be consumed, such as the cheese in the example at page 12. No where is there any disclosure of a polyhydroxalkanoate fluid which is suitable for injection as is required for the repair or augmentation of tissue in an animal or human. Therefore Eggink does not disclose each claimed element of the claims as required under 35 U.S.C. 102.

Marchessault

Marchessault does not even relate to fluidss which are suitable for injection or implantation into the body; Marchessault relates to a latex for making papers or films, and use of the films for purposes such as drug delivery (see page 3). However, the claims are drawn to a fluid for use in repair or augmentation of tissue. No such materials are disclosed.

Martin

Martin does not disclose a fluid containing a polyhydroxyalkanoate which is suitable for injection. Martin only discloses polyhydroxyalkanoates in solid form, which may be injected or

implanted in solid form. The only disclosure of the polyhydroxyalkanoates in liquid form is during processing, using solvents which clearly are not appropriate for injection into a human or animal.

Williams

Williams is the same with respect to the claims in issue as Martin.

In summary, the prior art fails to disclose the features of the independent claims: a fluid composition containing polyhydroxyalkanoate which is injectable into a human or animal. The prior art also fails to disclosure the features of the dependent claims, only a few of which the examiner appears to have examined. For example, no art has been cited which discloses an amorphous polyhydroxyalkanoate; no art has been cited which discloses a polyhydroxyalkanoate which is liquid at body temperature; no art has been cited with discloses polymers of the claimed molecular weights; and no art has been cited disclosing use in specific treatments, such as having a viscosity for use in treating arthritic knees.

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Accordingly, allowance of all claims 1-17 and 29-32 is earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the enclosed Amendment and all documents shown as being attached are being facsimile transmitted to the U. S. Patent and Trademark Office on the date shown below.

Date: July 25, 2002

Patrea L. Pabst

APPENDIX: Marked up Copy of Claims as Amended

1. (amended) A composition for the repair or augmentation of tissue in an animal or human, comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate which is injectable into a human or animal for repair or augmentation of tissue.

2. The composition of claim 1 wherein the polyhydroxyalkanoate is a liquid or wax at a temperature between about 20 and 25 °C.

3. The composition of claim 1 wherein the polyhydroxyalkanoate is liquid at the body temperature of the animal.

4. The composition of claim 1 wherein the polyhydroxyalkanoate is a liquid at about 37 °C.

5. The composition of claim 1 wherein the biocompatible fluid is a microdispersion of particles of the polyhydroxyalkanoate dispersed in a physiologically compatible liquid carrier.

6. The composition of claim 5 wherein the carrier is a second polyhydroxyalkanoate or an aqueous solution.

7. (amended) The composition of claim [1] 5 wherein the particles have a diameter of less than about 500 μm.

8. The composition of claim 7 wherein the diameter is less than about 50 μm.

9. The composition of claim 8 wherein the diameter is less than about 5 μm.

10. The composition of claim 1 wherein the polymer is derived from one or more monomers selected from the group consisting of 2-hydroxybutanoate, 3-hydroxyalkanoates, 3-hydroxyalkenoates, 4-hydroxyalkanoates, 4-hydroxyalkenoates, 5-hydroxyalkanoates, 5-hydroxyalkenoates, 6-hydroxyalkanoates, and 6-hydroxyalkenoates.

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12. (amended) The composition of claim 11 wherein the molecular weight is less than 50,000 as determined by gel permeation chromatography.

13. The composition of claim 1 having a viscosity between about 1 and 100,000 cP.

14. The composition of claim 13 having a viscosity between about 1 and 10,000 cP.

15. (amended) The composition of claim 1 further comprising [an agent selected from the group consisting of dyes, compounds with anti-microbial activity, anesthetics, adjuvants, anti-inflammatory compounds, surfactants, steroids, lipids, enzymes, antibodies, and hormones] a bioactive agent.

16. The composition of claim 1 further comprising a peptide or protein.

17. The composition of claim 1 wherein the polyhydroxyalkanoate is amorphous.

Please cancel claims 18-28.

29. (amended) A composition suitable for use in the treatment of osteoarthritic knees comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate, wherein the composition is suitable for use as a viscosupplement

30. The composition of claim 28 wherein the polyhydroxyalkanoate is amorphous.

31. (amended) A kit [of parts] comprising

(a) the composition of claim 1; and

(b) a means for delivering the composition to a patient.

32. The kit of claim 31 wherein the means for delivering comprises a needle and a syringe.

APPENDIX: Clean Copy of Claims as Amended

A 1 1. (amended) A composition for the repair or augmentation of tissue in an animal or human, comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate which is injectable into a human or animal for repair or augmentation of tissue.

2. The composition of claim 1 wherein the polyhydroxyalkanoate is a liquid or wax at a temperature between about 20 and 25 °C.

3. The composition of claim 1 wherein the polyhydroxyalkanoate is liquid at the body temperature of the animal.

4. The composition of claim 1 wherein the polyhydroxyalkanoate is a liquid at about 37 °C.

5. The composition of claim 1 wherein the biocompatible fluid is a microdispersion of particles of the polyhydroxyalkanoate dispersed in a physiologically compatible liquid carrier.

6. The composition of claim 5 wherein the carrier is a second polyhydroxyalkanoate or an aqueous solution.

A 2 7. (amended) The composition of claim 5 wherein the particles have a diameter of less than about 500 μm.

8. The composition of claim 7 wherein the diameter is less than about 50 μm.

9. The composition of claim 8 wherein the diameter is less than about 5 μm.

10. The composition of claim 1 wherein the polymer is derived from one or more monomers selected from the group consisting of 2-hydroxybutanoate, 3-hydroxyalkanoates, 3-hydroxyalkenoates, 4-hydroxyalkanoates, 4-hydroxyalkenoates, 5-hydroxyalkanoates, 5-hydroxyalkenoates, 6-hydroxyalkanoates, and 6-hydroxyalkenoates.

A3

11. .(amended) The composition of claim 1 wherein the polyhydroxyalkanoate has a molecular weight of less than 100,000 as determined by gel permeation chromatography.

12. (amended) The composition of claim 11 wherein the molecular weight is less than 50,000 as determined by gel permeation chromatography.

13. The composition of claim 1 having a viscosity between about 1 and 100,000 cP.

14. The composition of claim 13 having a viscosity between about 1 and 10,000 cP.

15. (amended) The composition of claim 1 further comprising a bioactive agent.

16. The composition of claim 1 further comprising a peptide or protein.

17. The composition of claim 1 wherein the polyhydroxyalkanoate is amorphous.

Please cancel claims 18-28.

A4

29. (amended) A composition suitable for use in the treatment of osteoarthritic knees comprising

a biocompatible, bioabsorbable fluid which comprises a polyhydroxyalkanoate, wherein the composition is suitable for use as a viscosupplement

30. The composition of claim 28 wherein the polyhydroxyalkanoate is amorphous.

A5

31. (amended) A kit comprising

(a) the composition of claim 1; and

(b) a means for delivering the composition to a patient.

32. The kit of claim 31 wherein the means for delivering comprises a needle and a syringe.